static responses will be largely determined by the identification and purification of specific neuropeptide receptors, the in situ analysis of receptor and receptor-gene regulation and the design of novel pharmacologic agonists and antagonists based on our understanding of receptor stereospecificity.

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Compliance in Taking Medications

MEDICAL COMPLIANCE has become a major factor in treating chronic disease. It is estimated that 50% of patients do not comply with their medical regimens. Noncompliance is especially a problem in treating patients with allergic disorders, as they frequently must take medication even when they are feeling well.

Compliance will vary in direct proportion to patients' understanding of a medical problem, their perceived benefit of a therapeutic plan, the possibility of medication side effects, the inconvenience of a therapeutic regimen and its cost.

To decrease the incidence of side effects, a new medication regimen should be initiated with the lowest dose possible, then the dosage titrated slowly up to the optimal therapeutic range (unless side effects occur). Potential side effects should be explained to patients. A written sheet, such as the American Medical Association's patient medication instructions or one designed by the physician, should be given to the patient.

It is important for physicians to explain simply why patients must take their medication in a specific manner. This explanation should be given in lay terms, and patients should be provided with clearly written instructions, including the name of the medication, its dosage and schedule.

A practical way to provide these written instructions is through the use of an inexpensive wallet-sized card called the Medical Management Card. This card has been used with success for years at the allergy clinic of the University of California, Irvine. Complimentary copies of the Medical Management Card can be obtained from Mark Havel, Tri-City Medical Center, 4002 Vista Way, Oceanside, CA 92056 or local Key Pharmaceutical representatives.

In addition to the above, using a simplified drug regimen that, where possible, emphasizes the use of once-a-day or twice-a-day medication will greatly increase the probability that a patient will use the medication regularly. Prescribing Uniphyl, a once-a-day theophylline compound, can facilitate compliance and will still be as efficacious as the standard twice-a-day theophylline preparation, Theo-Dur. Theophylline compliance can be monitored by using Acculevel assay, which gives results in 30 minutes.

A simplified drug regimen is especially important in the school-aged population, where medication is frequently missed if a dose has to be taken at school. In younger children (who are often unable to swallow a tablet), it is frequently difficult to administer a liquid preparation because of taste, problems with spillage and problems with dosing. Therefore, the use of a beaded capsule sprinkled over applesauce or other foods is frequently more convenient.

Physicians should be aware of the economics of a therapeutic plan, but not use generic substitutes to save costs if those products will not have the same therapeutic efficacy as the brand-name medication. This may be especially the case for certain long-acting, sustained-release theophylline preparations.

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Indications for Giving Immune Globulin Intravenously

THE CURRENT AVAILABILITY of safe intravenous immune globulin preparations has led to applications in various clinical situations. Intramuscular preparations have been used for decades for replacement therapy in antibody deficiency states, but only relatively small doses are tolerated. There is a delay in absorption from the injection site, and some proteolytic degradation may occur before the immunoglobulin is absorbed into the bloodstream. These problems do not exist with intravenously administered immune globulin.

Immune globulin therapy is indicated in patients with humoral immune defects who are unable to produce adequate amounts of IgG (serum IgG levels less than 400 mg per dl in older children and adults or a proved subclass deficiency). Immune globulin given intravenously is preferable to intramuscular preparations in patients with limited muscle mass or bleeding tendencies, those needing large, rapid increases in their serum IgG level or those in whom intramuscular therapy is poorly tolerated. Doses should be individually tailored to a patient's clinical response because susceptibility to infection does not always correlate with IgG serum levels. Generally, levels within one standard deviation of normal for a patient's age can be attained with 150 to 300 mg per kg body weight of immune globulin given intravenously every three weeks, depending on a patient's rate of catabolizing the immune globulin. Deficiency of one or more IgG subclasses in a patient with severe or recurrent infections can be successfully treated with intravenous administration of immune globulin provided the preparation contains adequate concentrations of the deficient subclass(es). Preparations with an IgG subclass distribution similar to that in normal human serum are preferable and are currently available in the United States from Cutter, Hyland and Sandoz laboratories. Prophylaxis or therapy with intravenous immune globulin may also be indicated when

there is a defect in a specific antibody formation to a particular infectious agent.

Immune globulin given intravenously in high doses has been found to promote a rapid rise in the platelet count in as many as 75% of patients with idiopathic thrombocytopenic purpura (ITP). Splenectomy can often be avoided or postponed in patients unresponsive to steroid therapy who would otherwide need an operation. Response rates and length of remission are more favorable in acute childhood forms of ITP. It is difficult to maintain remission in some cases of chronic ITP unless repeated doses of intravenous immune globulin are given, and this can become expensive and time consuming. Because it is not possible at this time to predict which patients with ITP will respond to immune globulin given intravenously, it may be administered when there is risk of life-threatening hemorrhage (platelet count $< 20,000$ per μl), during preparation for an operation, to control platelet deficiency hemorrhage or to avoid a splenectomy. Some patients who fail to respond to splenectomy benefit from intravenous immune globulin therapy. Immune globulin has been used in treating ITP during pregnancy, being administered to a mother before delivery and to a thrombocytopenic infant during the first several weeks of life until the platelet count has become stable.

Anaphylactic reactions have been associated with the intravenous administration of immune globulin in some patients with total IgA deficiency. These patients often form IgG, IgM or IgE (or all three) antibodies against the IgA present in many intravenous preparations of immune globulin. IgE antibodies appear to correlate best with the occurrence of anaphylaxis. If such therapy is indicated in such a patient, an intravenous preparation of immune globulin with a very low content of IgA should be used, preferably less than 5 μg per ml. At present, one preparation meeting this criterion is commercially available (Gammagard, Hyland).

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Leukotrienes

THE LEUKOTRIENES are a family of potent mediators of hypersensitivity and inflammation that are derived from the 5-lipoxygenation of arachidonic acid in mast cells, mononuclear phagocytes and polymorphonuclear leukocytes. Beyond a source in leukocytes and other inflammatory cells and the presence of three conjugated double bonds, for which the family name was selected, the leukotrienes share the same biosynthetic precursor, a requirement for additional polar substituents for expression of activity and oxidative mechanisms of inactivation. The parent 5,6-epoxyeicosatetraenoic acid, termed leukotriene (LT) A_4, is converted enzymatically either to a 5-hydroxy-6-*S*-glutathionyleicosatetraenoic acid designated leukotriene C_4 (LTC_4) and then by peptidolysis to the other sulfidopeptide leukotrienes LTD_4 and LTE_4 or to a 5,12-dihydroxyeicosatetraenoic acid called LTB_4. The principal pathway of inactivation of LTC_4, LTD_4 and LTE_4 is by peroxidation to the respective sulfones and of LTB_4 by ω-oxidation to 20-hydroxy-LTB_4 and 20-carboxy-LTB_4. Each of the leukotrienes now can be extracted and isolated in high yield by liquid chromatography and quantified by specific and sensitive radioimmunoassays.

LTC_4, LTD_4 and LTE_4 are potent vasoactive and smooth muscle contractile factors that together constitute the slow-reacting substance of anaphylaxis. Maximal constriction of human bronchi is evoked by concentrations of the sulfidopeptide leukotrienes 1/10,000 to 1/100 that of histamine. In addition, the pulmonary airway constriction is maintained for a longer time when the stimulus is leukotrienes than if it is histamine. Concentrations of sulfidopeptide leukotrienes too low to elicit bronchial constriction may decrease the threshold for responses to subsequent stimuli and thus create a hyperirritable state, as in asthma. LTB_4 is the most potent stimulus of polymorphonuclear leukocyte chemotaxis and other functions to be generated from arachidonic acid. LTB_4, like prostaglandin E_2, is immunosuppressive by way of specific actions on regulatory T lymphocytes. The effects of leukotrienes on leukocytes, blood vessels, smooth muscles and other tissues is mediated by distinct subsets of cellular receptors.

Leukotrienes are detected in tissues and fluids in relation to the expression of several types of hypersensitivity and inflammatory reactions. In the skin, LTB_4 predominates in patients with psoriasis and LTC_4 in cases of allergic reaction elicited by pollen proteins. LTC_4 and LTB_4 are found in the fluid of pulmonary airways of patients during attacks of asthma, whereas LTD_4 and LTE_4 attain high concentrations in cases of adult respiratory distress syndrome. LTB_4 is the principal mediator of neutrophilic reactions, as are typical of gout and spondyloarthritis. Although the establishment of functionally relevant concentrations of leukotrienes in these diseases is temporally related to the tissue reactions, no inhibitors or antagonists of sufficient specificity to confirm the relationship have been applied systematically.

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Childhood Asthma and Sinus Disease

TRIGGERING FACTORS that aggravate bronchial reactivity in patients with asthma continue to be described. In young children, lower respiratory tract infections, especially those due to respiratory viruses, are the most common inciting events; in older children, environmental allergens take on greater